

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 868, 870, and 882

[Docket No. 2003N-0468]

**Medical Devices; Effective Date of Requirement for Premarket Approval for
Three Class III Preamendments Devices**

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule; opportunity to request a change in classification.

SUMMARY: The Food and Drug Administration (FDA) is proposing to require the filing of a premarket approval application (PMA) or a notice of completion of a product development protocol (PDP) for the following three class III preamendments devices: Indwelling blood oxyhemoglobin concentration analyzer, cardiopulmonary bypass pulsatile flow generator, and the ocular plethysmograph. The agency also is summarizing its proposed findings regarding the degree of risk of illness or injury designed to be eliminated or reduced by requiring the devices to meet the statute's approval requirements and the benefits to the public from the use of the devices. In addition, FDA is announcing the opportunity for interested persons to request that the agency change the classification of any of the devices based on new information. This action implements certain statutory requirements.

DATES: Submit written or electronic comments by *[insert date 90 days after date of publication in the Federal Register]*. Submit requests for a change in classification by *[insert date 15 days after date of publication in the Federal Register]*. FDA intends that, if a final rule based on this proposed rule is issued,

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anyone who wishes to continue to market the device will need to submit a PMA within 90 days of the effective date of the final rule. Please see section XII of this document for the effective date of any final rule that may publish based on this proposal.

ADDRESSES: Submit written comments or requests for a change in classification to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to <http://www.fda.gov/dockets/ecomments>.

FOR FURTHER INFORMATION CONTACT: Joseph M. Sheehan, Center for Devices and Radiological Health (HFZ-215), Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850, 301-827-2974.

SUPPLEMENTARY INFORMATION:

I. Background—Regulatory Authorities

The Federal Food, Drug, and Cosmetic Act (the act), as amended by the Medical Device Amendments of 1976 (the 1976 amendments) (Public Law 94-295) and the Safe Medical Devices Act of 1990 (the SMDA) (Public Law 101-629), established a comprehensive system for the regulation of medical devices intended for human use. Section 513 of the act (21 U.S.C. 360c) established three categories (classes) of devices, depending on the regulatory controls needed to provide reasonable assurance of their safety and effectiveness. The three categories of devices are class I (general controls), class II (special controls), and class III (premarket approval).

Under section 513 of the act, devices that were in commercial distribution before May 28, 1976 (the date of enactment of the 1976 amendments), generally referred to as preamendments devices, are classified after FDA has: (1) Received a recommendation from a device classification panel (an FDA

advisory committee); (2) published the panel's recommendation for comment, along with a proposed regulation classifying the device; and (3) published a final regulation classifying the device. FDA has classified most preamendments devices under these procedures.

Devices that were not in commercial distribution prior to May 28, 1976, generally referred to as postamendments devices, are classified automatically by statute (section 513(f) of the act) into class III without any FDA rulemaking process. Those devices remain in class III and require premarket approval, unless and until the device is reclassified into class I or II or FDA issues an order finding the device to be substantially equivalent, in accordance with section 513(i) of the act, to a predicate device that does not require premarket approval. The agency determines whether new devices are substantially equivalent to previously offered devices by means of premarket notification procedures in section 510(k) of the act (21 U.S.C. 360(k)) and 21 CFR part 807.

Section 515(b)(1) of the act (21 U.S.C. 360e(b)(1)) established the requirement that a preamendments device that FDA has classified into class III is subject to premarket approval. A preamendments class III device may be commercially distributed without an approved PMA or a notice of completion of a PDP until 90 days after FDA issues a final rule requiring premarket approval for the device, or 30 months after final classification of the device under section 513 of the act, whichever is later. Also, a preamendments device subject to the rulemaking procedure under section 515(b) of the act is not required to have an approved investigational device exemption (IDE) (see 21 CFR part 812) contemporaneous with its interstate distribution until the date identified by FDA in the final rule requiring the

submission of a PMA for the device. At that time, an IDE is required only if a PMA has not been submitted or a PDP completed.

Section 515(b)(2)(A) of the act provides a proceeding to issue a final rule to require premarket approval shall be initiated by publication of a notice of proposed rulemaking containing: (1) The regulation, (2) proposed findings with respect to the degree of risk of illness or injury designed to be eliminated or reduced by requiring the device to have an approved PMA or a declared completed PDP and the benefit to the public from the use of the device, (3) an opportunity for the submission of comments on the proposed rule and the proposed findings, and (4) an opportunity to request a change in the classification of the device based on new information relevant to the classification of the device.

Section 515(b)(2)(B) of the act provides that if FDA receives a request for a change in the classification of the device within 15 days of the publication of the notice, FDA shall, within 60 days of the publication of the notice, consult with the appropriate FDA advisory committee and publish a notice denying the request for change in reclassification or announcing its intent to initiate a proceeding to reclassify the device under section 513(e) of the act. Section 515(b)(3) of the act provides that FDA shall, after the close of the comment period on the proposed rule and consideration of any comments received, issue a final rule to require premarket approval, or publish a document terminating the proceeding together with the reasons for such termination. If FDA terminates the proceeding, FDA is required to initiate reclassification of the device under section 513(e) of the act, unless the reason for termination is that the device is a banned device under section 516 of the act (21 U.S.C. 360f).

If a proposed rule to require premarket approval for a preamendments device is finalized, section 501(f)(2)(B) of the act (21 U.S.C. 351(f)(2)(B)) requires that a PMA or notice of completion of a PDP for any such device be filed within 90 days of the date of issuance of the final rule or 30 months after the final classification of the device under section 513 of the act, whichever is later. If a PMA or notice of completion of a PDP is not filed by the later of the two dates, commercial distribution of the device is required to cease.

The device may, however, be distributed for investigational use if the manufacturer, importer, or other sponsor of the device complies with the IDE regulations. If a PMA or notice of completion of a PDP is not filed by the later of the two dates, and no IDE is in effect, the device is deemed to be adulterated within the meaning of section 501(f)(1)(A) of the act, and subject to seizure and condemnation under section 304 of the act (21 U.S.C. 334) if its distribution continues. Shipment of devices in interstate commerce will be subject to injunction under section 302 of the act (21 U.S.C. 332), and the individuals responsible for such shipment will be subject to prosecution under section 303 of the act (21 U.S.C. 333). In the past, FDA has requested that manufacturers take action to prevent the further use of devices for which no PMA has been filed and may determine that such a request is appropriate for the class III devices that are the subjects of this regulation.

The act does not permit an extension of the 90-day period after issuance of a final rule within which an application or a notice is required to be filed. The House Report on the 1976 amendments states that:

[t]he thirty month 'grace period' afforded after classification of a device into class III * * * is sufficient time for manufacturers and importers to develop the data and

conduct the investigations necessary to support an application for premarket approval (H. Rept. 94–853, 94th Cong., 2d sess. 42 (1976)).

The SMDA added section 515(i) to the act requiring FDA to review the classification of preamendments class III devices for which no final rule has been issued requiring the submission of PMAs and to determine whether or not each device should be reclassified into class I or class II or remain in class III. For devices remaining in class III, the SMDA directed FDA to develop a schedule for issuing regulations to require premarket approval. The SMDA does not, however, prevent FDA from proceeding immediately to rulemaking under section 515(b) of the act on specific devices, in the interest of public health, independent of the procedures of section 515(i). Indeed, proceeding directly to rulemaking under section 515(b) of the act is consistent with Congress' objective in enacting section 515(i), i.e., that preamendments class III devices for which PMAs have not been required either be reclassified to class I or class II or be subject to the requirements of premarket approval. Moreover, in this proposal, interested persons are being offered the opportunity to request reclassification of any of the devices.

In the **Federal Register** of May 6, 1994 (59 FR 23731), FDA issued a notice of availability of a preamendments class III devices strategy document. The strategy set forth FDA's plans for implementing the provisions of section 515(i) of the act for preamendments class III devices for which FDA had not yet required premarket approval. FDA divided this universe of devices into three groups.

Group 1 devices are devices that FDA believes raise significant questions of safety and/or effectiveness but are no longer used or are in very limited use. FDA's strategy is to call for PMAs for all group 1 devices in an omnibus

section 515(b) of the act rulemaking action. In the **Federal Register** of September 7, 1995 (60 FR 46718), FDA implemented this strategy by proposing requiring the filing of a PMA or a notice of completion of a PDP for 43 class III preamendments devices. Subsequently, in the **Federal Register** of September 27, 1996 (61 FR 50704), FDA called for the filing of a PMA or a notice of completion of a PDP for 41 preamendments class III devices.

Group 2 devices are devices that FDA believes have a high potential for being reclassified into class II. In the **Federal Registers** of August 14, 1995 (60 FR 41986), and of June 13, 1997 (62 FR 32355), FDA issued an order under section 515(i) of the act requiring manufacturers to submit safety and effectiveness information on these group 2 devices so that FDA can make a determination as to whether the devices should be reclassified.

Group 3 devices are devices that FDA believes are currently in commercial distribution and are not likely candidates for reclassification. FDA intends to issue proposed rules to require the submission of PMAs for the 15 high priority devices in this group in accordance with the schedule set forth in the strategy document. In the **Federal Registers** of August 14, 1995 (60 FR 41984), and of June 13, 1997 (62 FR 32352), FDA issued an order under section 515(i) of the act for the 27 remaining group 3 devices requiring manufacturers to submit safety and effectiveness information so that FDA can make a determination as to whether the devices should be reclassified or retained in class III.

II. Dates New Requirements Apply

In accordance with section 515(b) of the act, FDA is proposing to require that a PMA or a notice of completion of a PDP be filed with the agency for class III devices within 90 days after issuance of any final rule based on this proposal. An applicant whose device was legally in commercial distribution

before May 28, 1976, or whose device has been found to be substantially equivalent to such a device, will be permitted to continue marketing such class III devices during FDA's review of the PMA or notice of completion of the PDP. FDA intends to review any PMA for the device within 180 days, and any notice of completion of a PDP for the device within 90 days of the date of filing. FDA cautions that, under section 515(d)(1)(B)(i) of the act, the agency may not enter into an agreement to extend the review period for a PMA beyond 180 days unless the agency finds that “* * * the continued availability of the device is necessary for the public health.”

FDA intends that, under § 812.2(d) (21 CFR 812.2(d)), the preamble to any final rule based on this proposal will state that, as of the date on which the filing of a PMA or a notice of completion of a PDP is required to be filed, the exemptions in § 812.2(c)(1) and (c)(2) from the requirements of the IDE regulations for preamendments class III devices will cease to apply to any device that is: (1) Not legally on the market on or before that date, or (2) legally on the market on or before that date but for which a PMA or notice of completion of a PDP is not filed by that date, or for which PMA approval has been denied or withdrawn.

If a PMA or notice of completion of a PDP for a class III device is not filed with FDA within 90 days, after the date of issuance of any final rule requiring premarket approval for the device, commercial distribution of the device must cease. The device may be distributed for investigational use only if the requirements of the IDE regulations regarding significant risk devices are met. The requirements for significant risk devices include submitting an IDE application to FDA for its review and approval. An approved IDE is required to be in effect before an investigation of the device may be initiated or

continued. FDA, therefore, cautions that IDE applications should be submitted to FDA at least 30 days before the end of the 90-day period after the final rule to avoid interrupting investigations.

III. Proposed Findings With Respect to Risks and Benefits

As required by section 515(b) of the act, FDA is publishing its proposed findings regarding: (1) The degree of risk of illness or injury designed to be eliminated or reduced by requiring that these devices have an approved PMA or a declared completed PDP, and (2) the benefits to the public from the use of the devices.

These findings are based on the reports and recommendations of the advisory committees (panels) for the classification of these devices along with any additional information that FDA has discovered. Additional information can be found in the following proposed and final rules published in the **Federal Register** on these dates: Anesthesiology devices, 21 CFR part 868 (44 FR 63292, November 2, 1979, and 47 FR 31130, July 16, 1982); cardiovascular devices, 21 CFR part 870 (44 FR 13284, March 9, 1979 and 45 FR 7903, February 5, 1980); and neurological devices, 21 CFR part 882 (43 FR 55639, November 28, 1978, and 44 FR 51725, September 4, 1979).

IV. Devices Subject to This Proposal

A. Indwelling Blood Oxyhemoglobin Concentration Analyzer (21 CFR 868.1120)

1. Identification

An indwelling blood oxyhemoglobin concentration analyzer is a photo electric device used to measure, in vivo, the oxygen carrying capacity of hemoglobin in blood to aid in determining the patient's physiological status.

2. Summary of Data

The Anesthesiology Device Classification Panel recommended that the indwelling blood oxyhemoglobin concentration analyzer intended to measure, in vivo, the oxygen carrying capacity of hemoglobin in blood to aid in determining the patient's physiological status be classified into class III based on the lack of published clinical data relating to the safety of, and the problems associated with this device. FDA agreed and continues to agree with the panel's recommendation that the device be classified into class III.

3. Risks to Health

a. *Inappropriate therapy*—Inaccurate measurement of the blood oxyhemoglobin concentration may cause an incorrect diagnosis leading to inappropriate therapy.

b. *Thrombus or embolus formulation*—If the analyzer materials are incompatible with the blood, thrombus or embolus (clot) formation may result.

c. *Electrical shock*—If the device is not designed properly, the patient may receive an electrical shock.

d. *Vascular occlusion*—If the device sensor is too large, it may occlude the blood vessel in which it is placed, thus stopping the blood flow through that vessel.

B. Cardiopulmonary Bypass Pulsatile Flow Generator (21 CFR 870.4320)

1. Identification

A cardiopulmonary bypass pulsatile flow generator is an electrically and pneumatically operated device used to create pulsatile blood flow. The device is placed in a cardiopulmonary bypass circuit downstream from the oxygenator.

2. Summary of Data

The Cardiovascular Devices Classification Panel recommended that the cardiopulmonary bypass pulsatile flow be classified into class III because it is potentially hazardous to life or health even when properly used and because there are insufficient data to establish the safety and effectiveness of the device. FDA agreed and continues to agree with the panel's recommendation. The agency notes that the device has fallen into disuse and that the published data are not adequate to demonstrate the safety and effectiveness of the device.

3. Risks to Health

a. *Cardiac arrhythmias or electrical shock*—Excessive electrical leakage current can disturb the normal electrophysiology of the heart, leading to the onset of cardiac arrhythmias. Electrical leakage current can also cause electrical shock to a physician during a catheterization or surgical procedure and this may lead to iatrogenic complications.

b. *Blood damage*—If the materials, surface finish, cleanliness, or improper mechanical design of this device are inadequate, damage to the blood may result.

c. *Thromboembolism*—Inadequate blood compatibility of the materials used in the device, inadequate surface finish and cleanliness, or improper mechanical design may lead to potentially debilitating or fatal gas emboli to escape into the bloodstream.

C. Ocular Plethysmograph (21 CFR 882.1790)

1. Identification

An ocular plethysmograph is a device used to measure or detect volume changes in the eye produced by pulsations of the artery, to diagnose carotid artery occlusive disease (restrictions on blood flow in the carotid artery).

2. Summary of Data

The Neurological Device Classification Panel recommended that the ocular plethysmograph be classified into class III because it is used to detect the life-threatening condition that occurs when the brain does not receive adequate blood flow through a carotid artery.

3. Risks to Health

- a. *Eye injury*—Excessive pressure can damage the eye.
- b. *Misdiagnosis*—The device may misdiagnose the presence or absence of carotid artery occlusion because of a poor relationship between pulsatile arterial blood flow changes and the degree of occlusion.
- c. *Infection*—Eye cups that are not sterile can cause infections.

V. PMA Requirements

A PMA for these devices must include the information required by section 515(c)(1) of the act. Such a PMA should also include a detailed discussion of the risks identified previously, as well as a discussion of the effectiveness of the device for which premarket approval is sought. In addition, a PMA must include all data and information on: (1) Any risks known, or that should be reasonably known, to the applicant that have not been identified in this document; (2) the effectiveness of the device that is the subject of the application; and (3) full reports of all preclinical and clinical information from

investigations on the safety and effectiveness of the device for which premarket approval is sought.

A PMA should include valid scientific evidence “obtained from well-controlled clinical studies, with detailed data,” in order to provide reasonable assurance of the safety and effectiveness of the device for its intended use (see 21 CFR 860.7(c)(2)).

Applicants should submit any PMA in accordance with FDA’s “Premarket Approval (PMA) Manual.” This manual is available upon request from FDA, Center for Devices and Radiological Health, Division of Small Manufacturers Assistance (HFZ–220), 1350 Piccard Dr., Rockville, MD 20850. This manual is also available on the Internet at <http://www.fda.gov/cdrh>.

VI. PDP Requirements

A PDP for any of these devices may be submitted in lieu of a PMA, and must follow the procedures outlined in section 515(f) of the act. A PDP should provide: (1) A description of the device, (2) preclinical trial information (if any), (3) clinical trial information (if any), (4) a description of the manufacturing and processing of the devices, (5) the labeling of the device, and (6) all other relevant information about the device. In addition, the PDP must include progress reports and records of the trials conducted under the protocol on the safety and effectiveness of the device for which the completed PDP is sought.

Applicants should submit any PDP in accordance with FDA’s “PDP Comprehensive Outline With Attachments.” This outline is available upon request from FDA, Center for Devices and Radiological Health, Office of Device Evaluation (HFZ–400), 9200 Corporate Blvd., Rockville, MD 20850. The outline

and other PDP information is also available on the Internet at <http://www.fda.gov/cdrh/pdp>.

VII. Request for Comments With Data

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments regarding this document. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

VIII. Opportunity to Request a Change in Classification

Before requiring the filing of a PMA or notice of completion of a PDP for a device, FDA is required by section 515(b)(2)(A)(i) through (b)(2)(A)(iv) of the act and 21 CFR 860.132 to provide an opportunity for interested persons to request a change in the classification of the device based on new information relevant to the classification. Any proceeding to reclassify the device will be under the authority of section 513(e) of the act.

A request for a change in the classification of these devices is to be in the form of a reclassification petition containing the information required by § 860.123 (21 CFR 860.123), including new information relevant to the classification of the device.

The agency advises that, to ensure timely filing of any such petition, any request should be submitted to the Division of Dockets Management (see **ADDRESSES**) and not to the address provided in § 860.123(b)(1). If a timely request for a change in the classification of these devices is submitted, the agency will, by *[insert date 60 days after date of publication in the Federal Register]*, after consultation with the appropriate FDA advisory committee and

by an order published in the **Federal Register**, either deny the request or give notice of its intent to initiate a change in the classification of the device in accordance with section 513(e) of the act and 21 CFR 860.130 of the regulations.

IX. Environmental Impact

The agency has determined under 21 CFR 25.30(h) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

X. Analysis of Impacts

FDA has examined the impacts of the proposed rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104–4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this proposed rule is consistent with the regulatory philosophy and principles identified in the Executive order. In addition, the proposed rule is not a significant regulatory action as defined by the Executive order and so is not subject to review under the Executive order.

If a rule has a significant economic impact on a substantial number of small entities, the Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because there have been no premarket submissions for these devices in the past 5 years, FDA has concluded that there is little or no interest

in marketing these devices in the future. Therefore, the agency certifies that the proposed rule, if issued as a final rule, will not have a significant impact on a substantial number of small entities. Therefore, under the Regulatory Flexibility Act, no further analysis is required.

XI. Paperwork Reduction Act of 1995

FDA tentatively concludes that this proposed rule contains no collections of information. Therefore, clearance by the Office of Management and Budget under the Paperwork Reduction Act of 1995 is not required.

XII. Proposed Effect Date

FDA is proposing that any final rule based on this proposal become effective 12 months after the date of its publication in the **Federal Register** or at a later date if stated in the final rule.

List of Subjects

21 CFR Parts 868, 870, and 882

Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR parts 868, 870, and 882 be amended as follows:

PART 868—ANESTHESIOLOGY DEVICES

1. The authority citation for 21 CFR part 868 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 371.

2. Section 868.1120 is amended by revising paragraph (c) to read as follows:

§ 868.1120 Indwelling blood oxyhemoglobin concentration analyzer.

* * * * *

(c) Date PMA or notice of completion of PDP is required. A PMA or notice of completion of a PDP is required to be filed with the Food and Drug Administration on or before [date 90 days after date of publication of the final rule in the **Federal Register**], for any indwelling blood oxyhemoglobin concentration analyzer that was in commercial distribution before May 28, 1976, or that has, on or before [date 90 days after date of publication of the final rule in the **Federal Register**], been found to be substantially equivalent to an indwelling blood oxyhemoglobin concentration analyzer that was in commercial distribution before May 28, 1976. Any other indwelling blood oxyhemoglobin concentration analyzer shall have an approved PMA or declared completed PDP in effect before being placed in commercial distribution.

PART 870—CARDIOVASCULAR DEVICES

3. The authority citation for 21 CFR part 870 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 371.

4. Section 870.4320 is amended by revising paragraph (c) to read as follows:

§ 870.4320 Cardiopulmonary bypass pulsatile flow generator.

* * * * *

(c) Date PMA or notice of completion of PDP is required. A PMA or notice of completion of a PDP is required to be filed with the Food and Drug Administration on or before [date 90 days after date of publication of the final rule in the **Federal Register**], for any cardiopulmonary bypass pulsatile flow generator that was in commercial distribution before May 28, 1976, or that has, on or before [date 90 days after date of publication of the final rule in the **Federal Register**], been found to be substantially equivalent to any

cardiopulmonary bypass pulsatile flow generator that was in commercial distribution before May 28, 1976. Any other cardiopulmonary bypass pulsatile flow generator shall have an approved PMA or declared completed PDP in effect before being placed in commercial distribution.

PART 882—NEUROLOGICAL DEVICES

5. The authority citation for 21 CFR part 882 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 371.

6. Section 882.1790 is amended by revising paragraph (c) to read as follows:

§ 882.1790 Ocular plethysmograph.

* * * * *

(c) Date PMA or notice of completion of PDP is required. A PMA or notice of completion of a PDP is required to be filed with the Food and Drug Administration on or before [date 90 days after date of publication of the final rule in the **Federal Register**], for any ocular plethysmograph that was in commercial distribution before May 28, 1976, or that has, on or before [date 90 days after date of publication of the final rule in the **Federal Register**], been found to be substantially equivalent to any ocular plethysmograph that was in commercial distribution before May 28, 1976. Any other ocular plethysmograph shall have an approved PMA or declared completed PDP in effect before being placed in commercial distribution.

Dated: 11/6/03

November 6, 2003.

Linda S. Kahan

Linda S. Kahan,
Deputy Director,
Center for Devices and Radiological Health.

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